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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/674,581	09/29/2003	Yuuki Tsutsui	019941-001810US	5398

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EXAMINER	
HISSONG, BRUCE D	
ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
05/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/674,581	TSUTSUI ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4, 7-10, 13-16, 19, 21-30* is/are pending in the application.

4a) Of the above claim(s) *21-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 7-10, 13-16, 19, 28-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. Applicants' response to the office action mailed on 12/14/2006, including arguments/remarks and amendments to the claims, was received on 3/14/2007 and has been entered into the record.

2. Claims 5-6, 11-12, and 17-18 were cancelled, and new claims 28-30 added in the amendment received on 3/14/2007. Therefore, claims 1-4, 7-10, 13-16, 19, and 21-30 are currently pending. Claims 21-27 are withdrawn as non-elected subject matter, and claims 1-4, 7-10, 13-16, 19, and 28-30 are the subject of this office action.

Claim Objections

Objection to claims 1, 8, 10, 13-14, and 19, as set forth on pages 2-3 of the office action mailed on 12/14/2006, is *withdrawn* in response to Applicants' amendments to the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1-4, 7-10, 13-16, and 19 *remain rejected*, and new claims 28-30 are also rejected, under 35 USC § 103(a) as being obvious in view of the combination of Staats *et al* ("Staats", WO 00/20028) and Takasu (*Kurume Med J.*, 2001, Vol. 48, p. 171-174), as set forth on pages 5-7 of the office action mailed on 12/14/2006.

The claims of the instant invention are drawn to a vaccine composition comprised of a vaccine antigen and an IFN-α, wherein the vaccine antigen can be a protein or peptide antigen, and the IFN-α can be natural or recombinant IFN-α, and present in an amount ranging from 0.5

– 5,000,000 IU. The claims are also drawn to the vaccine composition comprised of a vaccine antigen and IFN-α, wherein both the antigen and the IFN-α are administered nasally, and by the same route of administration, and wherein said composition induces antigen-specific antibodies in both the blood and at mucosal surfaces.

Staats teaches a method of eliciting an immune response by administration of a vaccine antigen and an adjuvant (see abstract, and claim 1). Staats teaches that the vaccine antigen can be either protein or peptide antigens, including protein/peptide antigens from a number of pathogenic organisms (see p. 21, line 11 – p. 23, line 2). Staats also teaches that various cytokines can be used as adjuvants (see p. 14, line 19 – p. 15, line 2, and claims 5-6). Furthermore, Staats teaches mucosal administration of the vaccine-adjuvant combination (claim 17), and also teaches that the vaccine-adjuvant induces both systemic (claim 22) and mucosal (claim 25) immune responses. Finally, by teaching that the vaccine and adjuvant are included together as a composition, Staats teach that the vaccine antigen and the adjuvant are administered at the same time and by the same route of administration. However, Staats is silent regarding the use of IFN-α as the adjuvant for any antigen-adjuvant combination or composition.

Takasu teaches that IFN-α is a potent adjuvant for increasing the immune response to various vaccine antigens. Specifically, Takasu discloses that co-administration of IFN-α with influenza virus peptide increased the cytotoxic T lymphocyte (CTL) response to the influenza virus peptide compared to vaccination with the influenza virus peptide alone (see p. 172-174, Figures 1-3).

In the response received on 3/14/2007, the Applicants argue that there is no motivation or suggestion provided in the disclosures of Staats and/or Takasu to create a vaccine composition comprising a vaccine antigen and further comprising IFN-α. The Applicants argue that Staats teaches a method wherein IFN-*gamma* is used, and that Staats does not teach the use of IFN-α. The Applicants also teach that Takasu does not teach or suggest nasal administration of IFN-α as an adjuvant with a peptide from influenza virus. In light of these deficiencies, the Applicants assert that there is no motivation to combine the teachings of Staats and Takasu.

These arguments have been fully considered and are not persuasive. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re*

Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, the combination of Staats and Takasu teaches methods of eliciting an immune response by mucosal administration of a vaccine and an adjuvant (Staats), and the effectiveness of IFN-a as a vaccine adjuvant (Takasu). Thus, one of ordinary skill in the art, knowing that IFN-α is an effective vaccine adjuvant, would have been motivated to use IFN-α as the adjuvant in the vaccine composition taught by Staats.

2. Claims 1-4, 7-10, 13-16, and 19 *remain rejected*, and new claims 28-30 are also rejected, under 35 USC § 103(a) as being obvious in view of the combination of Foster *et al* ("Foster", US 6,436,391) and Tovey (US 6,361,769), as set forth on pages 7-8 of the office action mailed on 12/14/2006.

The subject matter of the claims of the instant invention is discussed *supra*. Foster teaches the use of IFN-α as a vaccine adjuvant to increase B lymphocyte proliferation, and thus increase the effectiveness of vaccines (column 1, lines 52-56), and specifically recites co-administration of a vaccine with IFN-α, or alternatively, a composition comprised of IFN-α and a vaccine (column 1, lines 61-65). Foster is silent regarding mucosal administration of an IFN-α vaccine-adjuvant composition, and is also silent regarding specific amounts or doses of IFN-α.

Tovey teaches a method of stimulating host immunity by oromucosal administration of IFN-α (column 2, line 32 – column 3, line 28). Tovey discloses specific doses of IFN-α that can be oromucosally administered (column 3, line 15-20), and also teaches that IFN-α can be administered as an adjunct to other therapy (column 3, lines 21-22), and specifically mentions previous studies in which IFNs where orally administered to enhance the efficiency of vaccines (column 1, lines 61-66).

In the response received on 3/14/2007, the Applicants argue that neither Foster nor Tovey teach or suggest nasal administration of IFN-α with a vaccine antigen, or nasal administration of a vaccine antigen and IFN-α that induces both a vaccine antigen-specific antibody in the blood and a vaccine antigen-specific antibody secreted at the mucosal surface.

These arguments have been fully considered and are not persuasive. Tovey clearly teaches nasal administration of IFN-α (column 4, line 66 – column 5, line 1; see also column 7, lines 55-63). The combination of Foster and Tovey teaches the effectiveness of IFN-α as a vaccine adjuvant (Foster), and effective nasal administration of IFN-α (Tovey). Therefore, one of ordinary skill in the art would have been motivated to create a composition comprising a

vaccine antigen and IFN-α and administering said composition nasally, because the art teaches IFN-α is an effective adjuvant and can be administered nasally.

Conclusion

No claim is allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BDH
Art Unit 1646

ROBERT S. LANDSMAN, PH.D
PRIMARY EXAMINER